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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/613,018	07/07/2003	Ursula-Henrike Wienhues	2923-543	8627

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EXAMINER	
STEELE, AMBER D	
ART UNIT	PAPER NUMBER
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	01/25/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 01/25/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/613,018	WIENHUES ET AL.	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *5,8,13 and 15-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,7,9-12 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/776,188.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The amendment to the claims received on September 6, 2006 canceled claim 2 and amended claim 1.

Claims 1 and 3-24 are currently pending.

Claims 1, 3-4, 6-7, 9-12, and 14 are currently under consideration.

Election/Restrictions

2. This application contains claims (e.g. 16-18 and 23-24) drawn to an invention nonelected without traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.

Withdrawn Objections

3. The objection to Figure 1 is withdrawn in view of applicants' arguments and the amendment to the specification (brief description of the drawings on page 22) received on September 6, 2006.

4. The objection to the disclosure based on the lack of SEQ ID NOs: is withdrawn in view of the amendment to the specification received on September 6, 2006.

Withdrawn Rejections

5. The rejection of claims 1-7, 9-12, and 14 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 9-12, and 14 of U.S. Patent No. 6,613,530 B1 (Wienhues et al.) is withdrawn in view of the terminal disclaimer filed September 5, 2006.

6. The rejection of claims 1-4, 9-11, and 14 under 35 U.S.C. 102(b) as being anticipated by Hashida et al., Diagnosis of HIV-1 Infection by Detection of Antibody IgG to HIV-1 Urine with Ultrasensitive Enzyme Immunoassay (Immune Complex Transfer Enzyme Immunoassay) Using Recombinant Proteins as Antigens, Journal of Clinical Laboratory Analysis, 8(4): 237-246, 1994 is withdrawn in view of the amendment to claim 1 received on September 6, 2006.

Maintained Rejections

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. In addition, the text of the rejections have been altered to reflect the amendments to the claims received on September 6, 2006.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 3-4, 9-12, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hashida et al., Diagnosis of HIV-1 Infection by Detection of Antibody IgG to HIV-1 Urine with Ultrasensitive Enzyme Immunoassay (Immune Complex Transfer Enzyme Immunoassay) Using Recombinant Proteins as Antigens, Journal of Clinical Laboratory Analysis, 8(4): 237-246, 1994 and Formoso et al. WO 90/07119 published June 28, 1990.

For present claim 1 method step a), Hashida et al. teach incubating a urine sample (e.g. liquid sample), a solid phase, a first antigen for the anti-HIV-1 IgG (e.g. antibody) covalently

linked to an enzyme (e.g. marker group), a second antigen for the anti-HIV-1 IgG covalently linked to DNP which binds to anti-DNP antibody bound to the solid phase to form a complex which is schematically depicted in Figure 1, and also a third antigen may be utilized (please refer to Figure 1, Abstract section, and pages 237-243).

For present claim 1 method step b), Hashida et al. teach detecting the antibody bound to the antigens via fluorescence or color development (please refer to Materials and Methods section, Figures 1-13, and pages 239-243).

For present claim 1 method step b) and claims 3-4, Hashida et al. teach the antigen being conjugated (e.g. covalently bound) to both BSA (e.g. carrier) and enzyme labels (e.g. marker group) via various thiol and maleimide groups and either utilizing RT as antigen alone (e.g. multiple epitopes and multiple copies of the same amino acid groups and the first and second antigens are the identical amino acid sequence) or utilizing RT, p17, and p24 (e.g. multiple epitopes and multiple copies of the same amino acid groups) (e.g. $T(\text{-}P\text{-}L_m)_n$ or $(P\text{-})_nT(\text{-}L)_m$; please refer to Materials and Methods section, Figures 1-13, and pages 239-243).

For present claims 9-11, Hashida et al. teach that BSA or bovine serum albumin is coupled to the antigens (e.g. carrier; please refer to Material and Methods section).

For present claim 14, Hashida et al. teach that p17 (e.g. 131 amino acids), p24 (e.g. 231 amino acids), and RT (e.g. 1000 amino acids) are utilized as antigens and are produced via recombinant techniques (e.g. up to 1000 amino acids; please refer to Materials and Methods section).

However, Hashida et al. do not teach an antigen comprising multiple epitope regions of identical amino acid sequence or peptide sequences of 6-50 amino acids.

For present claim 1, Formoso et al. teach multimers and polymers of various peptides (e.g. antigens, epitopes, multiple epitope regions of identical amino acid sequence; please refer to entire specification particularly claims 2-9 and 11-18).

For present claim 12, Formoso et al. teach synthetic peptides conjugated through the C-terminus to a carrier protein which are typically about 5 to about 22 amino acids in length and preferably 11-20 amino acids or 15-17 amino acids in length (e.g. sequences of 6 to 50 amino acids; please refer to page 3, lines 22-32, page 4, lines 33-35, page 9, lines 24-36).

For the present elected species of SEQ ID No: 5, Formoso et al. teach peptides of HIV-1 gp41 with the amino acid sequence of 1-15 of present SEQ ID No: 5 (please refer to claims 2 and 11).

In addition, Formoso et al. teach that the carrier protein is preferably BSA, the peptides can be utilized in determining the presence of HIV-1 or HIV-2 antibodies in fluid samples, and that multiple peptides can be utilized in the ELISA, EIA, or RIA assays to determine the presence of HIV antibodies (please refer to pages 3-4 Summary of the Invention section and pages 8-17 Description of the Specific Embodiments section).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method for an ultrasensitive enzyme immunoassay taught by Hashida et al. with the shorter synthetic peptides either in multimeric or polymeric form taught by Formoso et al.

One having ordinary skill in the art would have been motivated to do this because Formoso et al. teach that synthetic peptides allow standardized antigen production, avoidance of nonspecificity resulting from contaminating proteins of *E. coli* (e.g. utilized by Hashida et al. for

antigen production), and reduce time of incorporating new antigens necessitated by mutation of HIV peptides which will improve tests for HIV specific antibodies (please refer to page 3, lines 7-20 of Formoso et al.). In addition, Hashida et al. teach that mutation of HIV proteins especially after prolonged drug treatment is a concern for the specificity of HIV antibody assays (please refer to page 244 of Hashida et al.).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the method for an ultrasensitive enzyme immunoassay taught by Hashida et al. with the shorter synthetic peptides either in multimeric ro polymeric form taught by Formoso et al. because Formoso et al. have shown the success of the screening and identification of antibodies using optimally immunoreactive peptides (please refer to page 11, lines 19-36 and page 12, lines 1-6 and Examples 1-20). In addition, the results of Hashida et al. show that the assay is more sensitive and specific than regular ELISA assays (please refer to Figures 1-16, particularly Figures 10 and 12-13; page 241-244 Diagnosis of HIV-1 Infection with Urine Samples section).

Therefore, the modification of the method for an ultrasensitive enzyme immunoassay taught by Hashida et al. with the shorter synthetic peptides either in multimeric ro polymeric form taught by Formoso et al. render the instant claims *prima facie* obvious.

Arguments and Response

10. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Hashida et al. and Formoso et al. for claims 1, 3-4, 9-12, and 14 were considered but are not persuasive for the following reasons.

Applicants contend that neither Hashida et al. nor Formoso et al. teach two or more identical peptides conjugated to the same carrier.

Applicants' arguments are not convincing since the teachings of Hashida et al. and Formoso et al. render the method for detection of an antibody of the instant claims *prima facie* obvious. It is the examiner's position that Formoso et al. teach multimers and polymers of peptides (e.g. repeating epitopes) which can be conjugated to a carrier (please refer to claims 1-18 and 21). Thus, the teachings of Hashida et al. and Formoso et al. render the instant claims *prima facie* obvious.

11. Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hashida et al., Diagnosis of HIV-1 Infection by Detection of Antibody IgG to HIV-1 Urine with Ultrasensitive Enzyme Immunoassay (Immune Complex Transfer Enzyme Immunoassay) Using Recombinant Proteins as Antigens, Journal of Clinical Laboratory Analysis, 8(4): 237-246, 1994 and Formoso et al. WO 90/07119 published June 28, 1990 as applied to claims 1, 3-4, 9-12, and 14 above, and further in view of Watts et al. U.S. Patent 5,437,983 filed February 1, 1993.

Hashida et al. teaches a method comprising incubating a urine sample, a solid phase, a first antigen covalently linked to an enzyme, a second antigen bound to the solid phase to form a complex and detecting the antibody bound to the antigens via fluorescence or color development. In addition, Hashida et al. teach the antigen being conjugated to both BSA and enzyme labels and either utilizing RT as antigen alone or utilizing RT (e.g. 1000 amino acids), p17 (e.g. 131 amino acids), and p24 (e.g. 231 amino acids) as antigens. Please refer to pages 237-243 of Hashida et al. Furthermore, Formoso et al. teach synthetic peptides conjugated through the C-

terminus to a carrier protein which are typically about 5 to about 22 amino acids in length and can be in multimeric or polymeric form (please refer to page 3, lines 22-32, page 4, lines 33-35, page 9, lines 24-36; claims 2-9 and 11-18).

However, Hashida et al. or Formoso et al. do not teach the hapten of digoxigenin and detectection of binding via anti-digoxigenin antibody.

For present claims 6-7, Watts et al. teach digoxigenin (e.g. cardiotonic glycosides) and antidigoxigenin antibody in binding assays with analytes and sbp or specific binding pairs and detecting signals (please refer to column 2, lines 1-18; column 3, lines 3-52; column 4, lines 15-35; column 5, lines 1-4; and Examples).

In addition, Watts et al. teach binding of sbps including antigens to labels to produce a signal producing system, utilizing beads as solid supports, performing the assay in a liquid medium, utilizing BSA, and screening for HIV related antibodies (please refer to column 4, lines 15-29; column 6, lines 41-67; column 7, lines 1-25, column 8, lines 9-51; column 9, lines 3-41; column 10, lines 22-31; column 11, lines 11-63).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the ultrasensitive enzyme immunoassay taught by Hashida et al. with the shorter synthetic peptides either in multimeric or polymeric form taught by Formoso et al. with the digoxigenin and anti-digoxigenin detection system taught by Watts et al.

One having ordinary skill in the art would have been motivated to do this because Watts et al. teach that various detection and labeling systems can be utilized including enzymatic, radioactive, and fluorimetric wherein one type of detection and labeling systems use is the digoxigenin and anti-digoxigenin detection system (please refer to column 1, lines 21-28).

Moreover, Formoso et al. and Hashida et al. both teach that various methods of detection and labeling can be utilized in antigen-antibody binding assays and the type of detection and labeling would be a choice of experimental design (Formoso: please refer to page 17, lines 6-9; Hashida: please refer to Figures 1-16).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the ultrasensitive enzyme immunoassay taught by Hashida et al. with the shorter synthetic peptides either in multimeric or polymeric form taught by Formoso et al. with the digoxigenin and anti-digoxigenin detection system taught by Watts et al. because Watts et al. have shown the success of using the detection and labeling systems of digoxigenin and anti-digoxigenin detection system (col. 17, lines 17-47).

Therefore, the modification of the ultrasensitive enzyme immunoassay taught by Hashida et al. with the shorter synthetic peptides either in multimeric or polymeric form taught by Formoso et al. with the digoxigenin and anti-digoxigenin detection system taught by Watts et al. render the instant claims *prima facie* obvious.

Arguments and Response

12. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Watts et al. for claims 6-7 further in view of Hashida et al. and Formoso et al. (claims 1, 3-4, 9-12, and 14) were considered but are not persuasive for the following reasons.

Applicants contend that Hashida et al., Formoso et al., or Watts et al. do not teach two or more identical peptides conjugated to the same carrier.

Applicants' arguments are not convincing since the teachings of Watts et al. further in view of the teachings of Hashida et al. and Formoso et al. render the method for detection of an

antibody of the instant claims *prima facie* obvious. It is the examiner's position that Formoso et al. teach multimers and polymers of peptides (e.g. repeating epitopes) which can be conjugated to a carrier (please refer to claims 1-18 and 21). Thus, the teachings of Hashida et al., Formoso et al., and Watts et al. render the instant claims *prima facie* obvious.

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ADS
January 18, 2007

MARK L. SHIBUYA
PRIMARY EXAMINER